

much less pain. She noted the tingling in her feet and pain in her right leg was alleviated. Her sleep patterns were the same. She reported there were no side effects taking DM/quinidine at a dosage of 30 mg/75 mg twice a day. At that point her dosages were increased to 60 mg of dextromethorphan and 75 mg of quinidine twice a day.

Two weeks later on May 19, the patient filled out a visual analog pain relief scale, indicating that the level of pain was substantially improved, now rated as 1 to 2 with 10 rated as pain as bad as it could be, indicating that she had obtained significant pain relief. The overall impression was that her pain was much better. She reported feeling well with no side effects. The tingling had diminished compared to the past when it occurred 3 to 4 times per week. On May 23 the patient reported her level of pain as between 0 and 1, which 0 indicating no pain. The patient then stopped taking the DM/quinidine and reported back on May 27 that she was well without any significant return of pain. On May 31, 1994 she reported that the tingling in feet and hands had returned and she was not sleeping as well. The patient then requested to be placed back on the medication.

Patient #2 was a 53-year-old male with painful sensations on his right side. This patient had suffered from a stroke in 1991. A CT scan at the time showed a left posterior cerebral infarct. The patient also had coronary artery disease and bypass surgery in 1991, and suffered from diabetes and hypertension. Neurological findings included visual and sensory loss, and right-sided weakness. Over the past 4 to 5 months, the patient had noted a buzzing sensation on his right side and an icy or heat sensation, which affected the right side of his face, arm, chest and leg. His left side was unaffected. This unpleasant sensation was particularly bothersome at night occurring for up to five minutes at a time, and off and on all day long. The buzzing sensation was generally always present. The sensation was uncomfortable, not very painful at times, but caused the patient a great deal of anxiety. In addition, the patient has noted some tingling in the bottom of both feet from time to time, a high pitched hum in his ears and lightheadedness when his head was tipped back. In addition, this patient had reported tinnitus.

The patient was assessed by the examining physician as having classic symptoms of Dejerine-Roussy Syndrome, which is pain emanating from a diseased thalamus secondary to stroke.

The patient initially assessed his pain on the visual analog scale as varying between 9 and 10 at peak period to between 5 and 6 at other times, with 10 indicating pain as bad as it could be. Six weeks after being placed on the medication at a dosage of 30 mg DM/75 mg quinidine twice a day, the patient indicated pain at between 7 and 8 at peak times, with pain between 3 and 4 at other times using the visual analog scale. At this time, the patient indicated the level of pain relief as between 2 and 3, with 0 indicating complete pain relief, and 10 indicating no pain relief. One week after stopping the medications, the patient indicated a return to a pain level at between 7 and 8.

Patient #3 was a 63 year old male who had been diagnosed with diabetes for 25 years. He also suffered from arthritis and hypertension. The patient complained of numbness in his hands for two years. In addition, the patient noted that his feet hurt for the past three years. Throbbing pain interfered with sleep and required pain pills. He also had pain at the tip of his buttocks and intermittent neck pain. The neurological examination was remarkable for markedly decreased pinprick sensation in the patient's feet and distal fingers, with normal position sense and slightly decreased

vibration sense. The clinical assessment was that the patient had primarily a sensory neuropathy secondary to his diabetes.

Prior to starting the DM-quinidine treatment at a dosage of 30 mg dextromethorphan and 75 mg quinidine at twelve hour intervals, the patient completed two visual analog scales describing his level of pain, one on April 11 and one shortly before beginning his medication on May 9. The patient initially rated his pain at between 5 and 6, and one month later as between 6 and 7, with 10 indicating the pain was as bad as it could be. The patient began taking DM-quinidine in the dosage of one tablet of 30 mg of dextromethorphan and 75 of quinidine twice a day.

On May 16 the patient noted via a telephone conversation that he felt lightheaded and his stomach was mildly upset, but he otherwise felt okay and he was continuing on the medication. The patient followed up in the office on May 23 and at that point, described that his pain was reduced from occurring nightly to only occurring occasionally, and was reduced overall to about 70-80% of what was previously experienced. He was not taking any other types of pain pills and had awakened only once at night from pain since being on the medication. He reported still having some intermittent light pain. Side effects were reported to be a little nausea, but not every day. At this time he rated his pain relief as between 1 and 2, with 0 indicating complete pain relief, and his current level of pain at between 1 and 2, with zero indicating no pain. The examining physician rated the patient's level of pain as much better.

On May 31 the patient reported pain in each foot during the previous week. He continued to take one tab of 30/75 DM/Quinidine. After two more weeks, he stopped taking the medication. On July 19, the patient completed another visual analog scale describing his current level of pain. He reported the level of pain as between 2 and 3, which remained lower than his initial assessment, even though he had discontinued his medication.

#### Example 8

##### Treatment of Tinnitus

Patient #2 from the pain study described in Example 7 also had suffered from chronic ringing in the ears, known as tinnitus, for a number of years. As a part of the pain study, this patient had taken 30 mg DM/75 mg quinidine capsules twice a day to relieve thalamic pain syndrome resulting from a stroke three years earlier. After about two weeks of taking the DM/quinidine capsules to relieve his pain, this patient reported an unexpected and total cessation of his chronic tinnitus. This evidence, together with published studies that NMDA receptors are found in the cochlear system which is the presumed site of the tinnitus disorder indicate that the DM/antioxidant combination is a promising therapy for tinnitus.

These examples demonstrate that the combination of dextromethorphan and an antioxidant such as quinidine are effective at treating intractable disorders, including intractable coughing, chronic pain, dermatitis, tinnitus and sexual dysfunction. Although this invention has been described with reference to the presently preferred embodiments, it is understood that various modifications can be made without departing from the spirit of the invention. According, the invention is limited only by the following claims.

We claim:

1. A method of increasing the effectiveness of dextromethorphan in treating chronic or intractable pain, com-

prising administering to a patient suffering from chronic or intractable pain a therapeutically effective dosage of dextromethorphan or a pharmaceutically acceptable salt thereof, in combination with a therapeutically effective dosage of a debrisoquin hydroxylase inhibitor.

2. The method of claim 1 wherein the debrisoquin hydroxylase inhibitor is selected from the group consisting of quinidine, quinine, and pharmaceutically acceptable salts thereof.

3. The method of claim 2 wherein quinidine is administered at a dosage not exceeding about 300 milligrams per day.

4. The method of claim 1 wherein the debrisoquin hydroxylase inhibitor is selected from the group consisting of disulfiram, fluoxetine, propranolol, nortriptyline, and pharmaceutically acceptable salts thereof.

5. A method of using dextromethorphan to treat chronic or intractable pain, comprising administering, to a patient suffering from chronic or intractable pain, dextromethorphan or a pharmaceutically acceptable salt thereof in combination with a debrisoquin hydroxylase inhibitor, wherein the dextromethorphan or salt thereof and the inhibitor are administered at combined dosages which render the dextromethorphan therapeutically effective in substantially reducing chronic or intractable pain, without causing unacceptable side effects.

6. The method of claim 5 wherein the debrisoquin hydroxylase inhibitor is selected from the group consisting of quinidine, quinine, and pharmaceutically acceptable salts thereof.

7. The method of claim 6 wherein quinidine is administered at a dosage not exceeding about 300 milligrams per day.

8. The method of claim 5 wherein the debrisoquin hydroxylase inhibitor is selected from the group consisting of disulfiram, fluoxetine, propranolol, nortriptyline, and pharmaceutically acceptable salts thereof.

9. A method of using dextromethorphan in treating tinnitus, comprising administering, to a patient suffering from tinnitus, dextromethorphan or a pharmaceutically acceptable salt thereof in combination with a debrisoquin hydroxylase inhibitor, wherein the dextromethorphan or salt thereof and the debrisoquin hydroxylase inhibitor are administered at combined dosages which render the dextromethorphan thereof therapeutically effective in substantially reducing tinnitus without causing unacceptable side effects.

10. The method of claim 9 wherein the debrisoquin hydroxylase inhibitor is selected from the group consisting of quinidine, quinine, and pharmaceutically acceptable salts thereof.

11. The method of claim 10 wherein quinidine is administered at a dosage not exceeding about 300 milligrams per day.

12. The method of claim 9 wherein the debrisoquin hydroxylase inhibitor is selected from the group consisting of disulfiram, fluoxetine, propranolol, nortriptyline, and pharmaceutically acceptable salts thereof.

13. A method for treating sexual dysfunction, comprising administering to a patient in need thereof dextromethorphan or a pharmaceutically acceptable salt thereof in combination with a debrisoquin hydroxylase inhibitor, at combined dosages which render the dextromethorphan thereof therapeutically effective in treating the sexual dysfunction.

14. The method of claim 13 wherein the patient is a male who suffers from priapism or premature ejaculation.

15. The method of claim 13 wherein the debrisoquin hydroxylase inhibitor is selected from the group consisting of quinidine, quinine, and pharmaceutically acceptable salts thereof.

16. The method of claim 15 wherein quinidine is administered at a dosage not exceeding about 300 milligrams per day.

17. The method of claim 13 wherein the debrisoquin hydroxylase inhibitor is selected from the group consisting of disulfiram, fluoxetine, propranolol, nortriptyline, and pharmaceutically acceptable salts thereof.

18. A unit dosage formulation for treatment of chronic or intractable pain, comprising:

(a) dextromethorphan or a pharmaceutically acceptable salt thereof, and,

(b) a debrisoquin hydroxylase inhibitor, in a combined form that is designed for oral ingestion by humans, wherein the dextromethorphan or salt thereof and the debrisoquin hydroxylase inhibitor are present at a combined dosage which renders the dextromethorphan therapeutically effective in substantially reducing chronic or intractable pain, without causing unacceptable side effects.

19. The unit dosage formulation of claim 18, comprising a digestible capsule which encloses the dextromethorphan or pharmaceutically acceptable salt thereof and the debrisoquin hydroxylase inhibitor.

20. The unit dosage formulation of claim 18, wherein the debrisoquin hydroxylase inhibitor is selected from the group consisting of quinidine, quinine, and pharmaceutically acceptable salts thereof.

21. The unit dosage formulation of claim 20, wherein the dosage of quinidine is 300 milligrams/day or less.

22. The unit dosage formulation of claim 18, wherein the debrisoquin hydroxylase inhibitor is selected from the group consisting of disulfiram, fluoxetine, propranolol, nortriptyline, and pharmaceutically acceptable salts thereof.

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